Court File No.: 05-CV-303001PD2

ONTARIO
SUPERIOR COURT OF JUSTICE

BETWEEN:

CANWEST MEDIAWORKS INC.

Applicant

and

ATTORNEY GENERAL OF CANADA

Respondent

REPLY AFFIDAVIT OF STEVEN G. MORGAN

I, **STEVEN G. MORGAN**, of the City of Vancouver in the Province of British Columbia, **AFFIRM AND SAY AS FOLLOWS**:

1. I have provided evidence in this matter on behalf of the Attorney General of Canada in an affidavit sworn 6 July 2006. My qualifications to provide this evidence, which includes, among other things, expert evidence on pharmaceutical policy and economics, are fully described therein.

2. The purpose of this affidavit is to provide points of clarification and comments regarding some of the evidence presented by CanWest MediaWorks Inc. in the matter of CanWest MediaWorks Inc v. Attorney General of Canada. In this affidavit, I will respond to the evidence of Professor Julie Donohue and that of Professor Richard Frank. Where I have quoted from the opinions and findings of other authors in my response to these affidavits, they are widely accepted as

experts in the matters on which they have written and their statements reflect my own opinion as well. Where I refer to sources that are not attached, the references for them are set out in a Bibliography attached as Exhibit 1 to this affidavit.

A. REPLY TO THE AFFIDAVIT OF PROFESSOR JULIE DONOHUE

1) Drugs heavily advertised with DTCA

3. As evidence regarding the nature and type of drugs most heavily advertised with DTCA, Professor Julie Donohue's affidavit draws heavily on a study by Toshiaki Iizuka that was published in the Journal of Industrial Economics. The study has a number of limitations that are not discussed by Professor Donohue. Iizuka studied only three therapeutic categories that were not chosen to be representative of the pharmaceutical market; Iizuka employed a US Food and Drugs Administration (FDA) measure of *potential* but not *actual* drug quality; Iizuka reassigned "high quality" status to many drugs the US FDA had assigned "low quality" to; and Iizuka excluded from his statistical analyses information pertaining to the marketing and quality of all drugs first approved for sale before 1982. In my opinion, these four limitations are significant, and in relying on the study, Professor Donohue draws conclusions regarding the nature of drugs advertised and the conditions for which they are advertised based on evidence from seriously flawed research.

4. Professor Donohue begins her discussion of the Iizuka paper immediately following an unsubstantiated criticism that studies assessing the

content of DTCA advertisements may not provide a representative view of the types of drugs advertised. Yet, the study by Iizuka was not designed to provide representative information about DTCA. It pertained only to three therapeutic categories of drug—"central nervous system agents," "respiratory agents," and "renal and genitourinary agents"—that account for less than half of the pharmaceutical market. These drug categories were not chosen to be representative but were instead chosen for convenience: to quote Iizuka, "I limit my samples to these categories largely due to the high cost of constructing the data set. While the estimation results may or may not extend to the remaining categories, these categories represent roughly 46% of industry sales in 1996 (S&P [1999])." [(Iizuka 2004) fn 12, p 359]. As such, even if it were an ideally designed study (which it was not), one cannot draw general conclusions from the findings of Iizuka's research.

5. The measure of product quality is one of the study design weaknesses in Iizuka's research. Iizuka assigned each drug to a "high" or "low" product quality category based, in part, on whether the US FDA had given the initial application to sell the drug a priority review. Professor Donohue asserts in paragraph 23 of her affidavit that products receiving such a review by the FDA "...may either be more efficacious than existing treatments, more user friendly (e.g., easier dosing scheme), or safer (lower incidence of side effects)." This statement is correct insofar as such products "*may*" have these desirable characteristics. It is also true that these drugs "*may not*" have these desirable characteristics because the

FDA must decide whether to conduct a priority review based on *potential* not *actual* comparative safety and efficacy of products.

6. Priority review status is a categorization given to determine the length of time the US FDA will take to complete the review of an application for product licensing. Applications for drugs that have greater potential to be a breakthrough in treatment are eligible for expedited review (see, Manual of Policies and Procedures for the FDA Center for Drug Evaluation and Research http://www.fda.gov/cder/mapp.htm). Because the priority status of a drug review must be assigned before the review itself (that is, before clinical trials data are thoroughly evaluated by FDA experts), the FDA assigns priority review not based on *proven* advances in efficacy, safety or convenience but based on the *potential* for a drug to provide such. Thus, based on Iizuka's methods for assigning drugs to a "high quality" category, VIOXX (generic name, rofecoxib) would be deemed a "high quality" drug because it had received a priority review by the US FDA. I mention this not to comment on the FDA's priority review process itself, but to illustrate the fact that an FDA priority review is not a reliable indicator of actual drug quality. Iizuka's research on the nature of drugs most heavily advertised therefore does not provide reliable evidence in support of claims that higher quality medicines are advertised more intensively than lower quality medicines.

7. Iizuka also reassigned many drugs into his "high quality" category even though they had been given a standard review by the US FDA. Specifically, Iizuka assumed that if one drug within a drug class had previously been granted

information. This includes Professor Donohue's conclusions that DTCA is most intensive for drugs of highest quality and that DTCA is most intensive for drugs to treat conditions that are most under-treated. Such conclusions are simply not substantiated by reliable research evidence.

2) Brand and Class Effect

10. Professor Donohue's conclusions regarding the potential consumer welfare benefits of DTCA are based in part on the assertion summarized in paragraph 67 of her affidavit that "... spending patterns on DTCA and economic studies of the demand effects of advertising suggest that it has market expanding rather than business stealing effects." In paragraphs 37 to 42 of her affidavit, Professor Donohue reviews literature concerning the market share effects of DTCA. That review of literature ignored or downplayed evidence inconsistent with the market expanding hypothesis.

11. In support of the market expanding hypothesis, Professor Donohue cites a study conducted by Professors Rosenthal, Berndt, Donohue, Epstein and Frank (Rosenthal, Berndt et al. 2003). Professor Donohue states she and her colleagues did not find a statistically significant relationship between DTCA and market share for the five drug classes analyzed in that study. It should be noted, however, that the authors wrote the following caveats about this 'non-finding' in their published paper: "both DTCA and detailing parameter estimates for the individual product demand models are neither robust nor precisely estimated." [(Rosenthal, Berndt et al. 2003) page 21] Thus, the study provides only tentative

support for the market expanding hypothesis. A conclusion that this hypothesis is supported by reliable research evidence would require that the balance of all other available research studies also supports it. The evidence does not.

12. A further important detail about the study design used by Professors Rosenthal, Berndt, Donohue, Epstein and Frank is that they only included information about six drugs from the therapeutic category of antidepressants. The six antidepressants included in their study were as follows: fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa), venlafaxine (Effexor), and nefazodone (Serzone) [Table 1.1 of (Rosenthal, Berndt et al. 2003)]. By focusing on these six drugs, the researchers ignored information about the use and cost of other medicine also used in the management of depression. As such, the paper by Rosenthal, Berndt, Donohue, Epstein and Frank lacks the data necessary to draw such a conclusion regarding market expanding versus business stealing effects of DTCA.

13. Two of Professor Donohue's studies on antidepressants—(Donohue and Berndt 2004; Donohue, Berndt et al. 2004)—also focused on the same selection of antidepressant drugs as the paper by Rosenthal, Berndt, Donohue, Epstein and Frank (Rosenthal, Berndt et al. 2003). [Details regarding the medicines included can be found on page 1177 of Donohue, Berndt et al. 2004 and on page 188 of Donohue and Berndt 2004.] As the following quote from Professor Donohue's work makes clear, the choice of these six drugs was based

on access to promotional data and resulted in the exclusion of many antidepressant drugs for which there is little or no DTCA:

> "We did not have access to promotional spending data on (and thus did not include) SSRIs that did not have an indication for depression (i.e., Luvox [fluvoxamine]); antidepressants that had generic equivalents at the time of the study (i.e., Desyrel [trazodone]); older-generation medications, such as tricyclic antidepressants; or products that represented a small share of the antidepressant market or products used primarily to treat conditions other than depression (i.e., Remeron [mirtazapine] and Wellbutrin [buproprion], respectively). None of these medications was advertised to consumers, and thus we do not include them in the study." [(Donohue and Berndt 2004) page 117]

14. Given that the work by Professor Donohue and her colleagues excluded drugs that were not heavily advertised, if at all, to consumers, economic theory would predict that the business stealing effects found in their studies of antidepressant use were likely understated because some of the apparent market expansion effects (for the 'class' of the six advertised brands) were actually just a matter of the advertised brands stealing business from the unadvertised antidepressants that had not been taken into consideration in her analysis. This significantly reduces the likelihood that DTCA observed in the studies by Professor Donohue and her colleagues was a net benefit to patients.

15. The omission of other therapeutic options from the analyses in the work by Professor Donohue and colleagues is a serious limitation that may bias their findings in favour of finding market expanding effects over market share

effects. The three aforementioned studies—(Donohue and Berndt 2004; Donohue, Berndt et al. 2004) (Rosenthal, Berndt et al. 2003)—do not contain enough information to rule out the possibility that DTCA for the six antidepressants that were included in the analyses did not simply reduce use of other antidepressants that might have been appropriate treatment options.

16. In paragraph 38, Professor Donohue refers to three studies of advertising in specific drug classes that found "either no association between DTCA advertising expenditures and prescription choice within the class, or very small effects relative to those of detailing." It would be more complete to say that two of these three studies found a positive association between DTCA and market share and that the one study that did not find an association between DTCA and market share is an unpublished working paper that has not been subject to peer review. Thus, the balance of the limited evidence that Professor Donohue cites in her arguments about market share effects does not support her conclusion that the effects of DTCA are primarily market expanding rather than business stealing.

17. In summary, the conclusions that Professor Donohue drew in paragraphs 40 and 67 with regard to the market expanding versus business stealing effects of DTCA are not supported by the research evidence she has cited. Her conclusions regarding market expanding versus business stealing effects of DTCA are also not supported by the balance of all other published

research evidence that I systematically reviewed in preparation for and summarized in my affidavit dated 6 July 2006.

B. REPLY TO THE AFFIDAVIT OF PROFESSOR RICHARD FRANK

1) Association between US DTCA and US Prescription Drug Expenditures

18. In paragraph 20 of Professor Richard Frank's affidavit, he notes that the analytic approach that I used to investigate the association between US DTCA and US prescription drug expenditures (relative to Canadian prescription drug expenditures) is frequently applied in economics. Professor Frank also notes that these methods are often used with careful attention to other key factors that might affect the analysis.

19. In preparation of my affidavit, I retrieved and assessed data regarding a wide variety of factors that might have been an underlying cause of the strong association between US DTCA per capita and the difference between per capita prescription drug expenditures in the US and Canada. For parsimony, I did not provide all of the data series in my original affidavit; rather, in paragraph 98 of my affidavit, I summarized these efforts by reporting that no changes in the pharmaceutical sector other than the recent rise in US DTCA could explain the timing, nature and magnitude of the recent divergence in prescription drug expenditure levels between the two countries.

20. The analysis that I did in preparation of my initial affidavit was subsequently peer-reviewed and published on 18 April 2007 in the medical

journal, Open Medicine. The appendix of the published version of my analysis included charts depicting many potential influences on the measured association between US DTCA and US prescription drug expenditures that I had explored in preparation of my affidavit; none were a significant influence. This published journal article is attached as Exhibit 2 to this affidavit. Specific figures are also attached as Exhibits 3, 4, and 5.

2) Out-of-pocket costs in the US

21. In paragraph 21 of his affidavit, Professor Frank discusses and provides selected data regarding the percentage of drug costs borne out of pocket by US consumers. In my opinion, and as is generally accepted practice in economic research, it is important to provide the complete series of such data so that trends in drug financing that occurred prior to the rise in DTCA can be compared to trends in drug financing that occurred after the rise in DTCA.

22. Although the publicly available data series actually extends as far back as 1960, Professor Frank's affidavit contains data only for the period of 1990 to 2003. Exhibit 3 attached to this affidavit provides a complete illustration of the data series that Professor Frank gave a selected snapshot of. As is clear from the complete data series, out-of-pocket spending has represented a steadily declining share of US expenditures on prescription drugs since 1960. Moreover, the rate at which out-of-pocket costs fell as share of total costs began to slow down in 1996.

23. Professor Frank also did not provide Canadian data on out-of-pocket drug costs. I provide the best available Canadian data on this variable, which unfortunately span only from 1988 to 2005, in Exhibit 4. It is notable from the Canadian data that out-of-pocket charges fluctuated from 24.2 percent of drug costs in 1988 to 20.4 percent in 1992 and back up to 25.1 percent in 1997. Out-of-pocket charges then fell from 25.1 percent of total Canadian drug costs in 1997 to 19.6 percent in 2005. What is important here is the fact that, like in the US, out-of-pocket drug costs were falling as a share of drug expenditures in Canada during the time period that US DTCA was increasing and US prescription drug expenditures were rising (relative to Canada). Unlike the US, the (limited) Canadian data do not show a steady decline in out-of-pocket drug costs as a share of total drug expenditure prior to 1996.

24. The selected snapshot of data provided by Professor Frank could give the impression that (1) the changes in out-of-pocket prescription drug financing in the US during the 1990s represented a new trend, (2) that this new trend toward reduced out-of-pocket payment occurred at the same time that US DTCA began to grow rapidly, and (3) that this new trend toward reduced out-of-pocket payment in US prescription drug financing was responsible for the contemporaneous growth in US prescription drug expenditures per capita as compared to Canadian prescription drug expenditures per capita.

25. With the benefit of the complete data series, it is clear that these impressions that might be given by the data series provided by Professor Frank

would be false. The logic that Professor Frank uses is not in question. But if the logic is applied with the complete data, then to the extent that US demand has been increasing as a result of the decline in out-of-pocket payment as a share of total US expenditure on prescription drugs, this response would have occurred relatively continuously from 1960 onward, and would have slowed down after 1996.

26. In conclusion, Professor Frank referred to changes in out-of-pocket drug costs in the US during the period of 1990 to 2003 as a potentially fatal flaw in the research I provided with regard to the association between US DTCA and US prescription drug expenditures relative to Canadian prescription drug expenditures. I disagree. The data provided in Professor Frank's affidavit give a selected snapshot that could lead to false conclusions. In preparation for my affidavit, I had explored all available data on trends in out-of-pocket drug costs in the US (and Canada) along with a wide variety of other factors that might have influenced the recent rise in US prescription drug expenditures relative to Canada. The analysis I conducted has since been peer reviewed and published in a medical journal.

3) Other influences on US and Canadian prescription drug expenditures

27. In paragraph 23 of his affidavit, Professor Frank discusses and provides reference to data regarding prescription drug expenditures as a share of total health care spending in Canada and the US, arguing that my presentation of the data was imbalanced and potentially misleading. I disagree. As discussed

above, in preparation of my affidavit, I sought out and analysed data concerning major health, economic and demographic factors that might otherwise explain the association found between US DTCA and US prescription drug expenditures relative to Canada.

28. My peer-reviewed article on this matter (published in April 2007), attached as Exhibit 2, contained figures illustrating 17 different data series regarding a wide range of health care, economic and demographic factors that might conceivably have been the 'true' underlying cause for the close association between US DTCA and US prescription drug expenditures (relative to Canadian prescription drug expenditures). Exhibit 5 reproduces those data with a detailed data legend. Each data series is indexed such that the value in 1995 is equal 1.00 and the value for all other years is expressed relative to that which occurred in 1995. The legend in Exhibit 5 shows the percentage change in each variable between 1995 and 2005.

29. Presenting the data as in Exhibit 5 allows all of the data series to be compared on the same scale by illustrating the relative extent to which each health care, economic and demographic factor had changed before and after 1995. Upon observation of the data, it will be clear that, other than US DTCA per capita, none of the 17 data series provided bear a close association with the growth in the difference in prescription drug expenditures per capita between the US and Canada observed since 1995. Therefore, as summarized in my initial affidavit, no changes in the health or pharmaceutical sector other than the recent

rise in US DTCA could explain the timing, nature and magnitude of the recent divergence in per capita prescription drug expenditures between the two countries.

4) Counterfactuals for DTCA studies

30. In paragraphs 30 and 31 of his affidavit, Professor Frank makes the point that Canadians already observe some DTCA advertising through US media. This is correct. He then argues that extrapolating US-based findings would be incorrect because the US studies compare the impact of DTCA against the counterfactual of no DTCA at all. However, several of the studies that Professor Frank cites to make his argument actually use within-USA variation in DTCA intensity across regions and over time to measure the impact of such advertising on patient request and related drug utilization and expenditure.

31. Even the study that Professor Frank was a co-author on used temporal variation in DTCA to measure the impact of high versus low DTCA advertising within the US: to quote that study, "We divided promotional spending into quartiles and calculated odds ratios (ORs) using the lowest quartile as the reference group" [(Donohue, Berndt et al. 2004) page 1178]. To be clear: these studies compare "high versus low DTCA" not "some versus no DTCA" as Professor Frank suggested in his affidavit.

32. Such studies are not methodologically incorrect. But they, along with the Canada-US comparative research by Barbara Mintzes and colleagues and

my Canada-US comparative analysis of population-level data, do establish the fact that there is a close relationship between DTCA intensity and the level of drug utilization and expenditure that is induced by it. The greater the amount of DTCA a population is exposed to—even just moving from 'low DTCA' to 'high DTCA' over time or across regions of a country—the greater the impact on prescription drug utilization, choices and expenditures. Thus, findings from the body of research that shows that US DTCA has had a significant impact on prescription drug utilization, prescription drug expenditures, market shares for advertised brands, and use of physician services still informs policy regarding the potential impact of increased DTCA in Canada. All of these outcomes can be expected to increase along with increases in the amount of DTCA in Canada.

5) The Study by Mintzes and Colleagues

33. In paragraph 22 Professor Frank calls into question my review of and reliance on the work by Barbara Mintzes and colleagues, stating "Since this study compares people and places that differ in numerous ways other than the level of exposure to DTC advertising (like culture, insurance arrangements), attributing all differences in the levels and patterns of prescribing to DTC advertising may be quite misleading." This statement may give an impression about the study that is factually incorrect. Consider the following quote, taken directly from the methods section of the paper by Mintzes and colleagues:

> "We examined differences between the 2 samples in self-reported advertising exposure, rates of drug requests and prescribing rates, after adjusting for age, sex, self-reported health status, income and

> education, and whether patients paid for drugs fully, partially or not at all. Questions about prescribing were also adjusted for physicians' sex and number of years since graduation. We used a generalized estimation equation (GEE) to adjust for correlation between patients of the same physician." [(Mintzes, Barer et al. 2003) page 406]

34. That is, the study by Mintzes and colleagues was designed to take into account the various ways in which patients in the two cities (Vancouver and Sacramento) might differ; it was also designed to take into account the various ways in which the physician practices might differ. Therefore, Professor Frank's criticism that the study attributed all prescribing differences to DTC advertising is unfounded.

6) Literature on the impact of DTCA

35. Professor Frank suggests in his affidavit that my review of the literature was selective and ignored important findings. I disagree. As is considered best practice for reviewing research to inform policy or clinical practice, I conducted a systematic review of the literature in preparation of my affidavit. Despite the hopes of their authors, it is seldom the case that any single study is definitive. It is therefore most appropriate to turn to systematic reviews of literature to determine what can be concluded from a body of critically appraised evidence rather than relying on single studies.

36. Being systematic ensures that all relevant evidence is found and that undue weight is not placed on studies that are not robust or not properly

estimated. In preparation of my affidavit, I updated and expanded a previously published systematic review of the literature on the impacts of DTCA (Gilbody, Wilson et al. 2005). In doing so, I employed an Information Specialist of the Program in Pharmaceutical Policy at the UBC Centre for Health Services and Policy Research who holds a masters degree in Library and Information Sciences to assist me in conducting a comprehensive search that identified 1774 unique titles related to the subject area.

37. Using a study inclusion and appraisal protocol designed to update and expand the study by Gilbody and colleagues, we identified 35 potentially relevant articles from the list of 1774 unique titles; critically apprised all 35 of articles; and summarized the findings of 19 unique studies that met appraisal criteria. I was personally involved in every stage of this review and can therefore be sure that no evidence was deliberately ignored or down-played. The review methods and findings were discussed in my affidavit dated 6 July 2006, and the review and the summary of it included the specific study that Professor Frank suggests was ignored—see Appendix 1 and Table 3 of my affidavit dated 6 July 2006.

38. In light of the systematic approach that I took to reviewing available evidence concerning the impact of DTCA, I can conclude with confidence that the findings reported in my affidavit represent an unbiased account of the body of research knowledge. On balance, published research shows that DTCA increases prescription drug utilization, prescription drug expenditures, market shares for advertised brands, and the use of physician services and other health

care services. There is no reliable evidence showing that drugs more intensively advertised using DTCA are of higher quality than those advertised less intensively with DTCA or those for which DTCA is not used. There is no reliable evidence showing that the drugs more intensively advertised are those for under-treated conditions when compared to drugs advertised less intensively with DTCA or those for which DTCA is not used.

AFFIRMED before me at the City of Vancouver, in the Province of British Columbia this 26th day of November, 2007.

(Commissioner for Taking Affidavits)

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